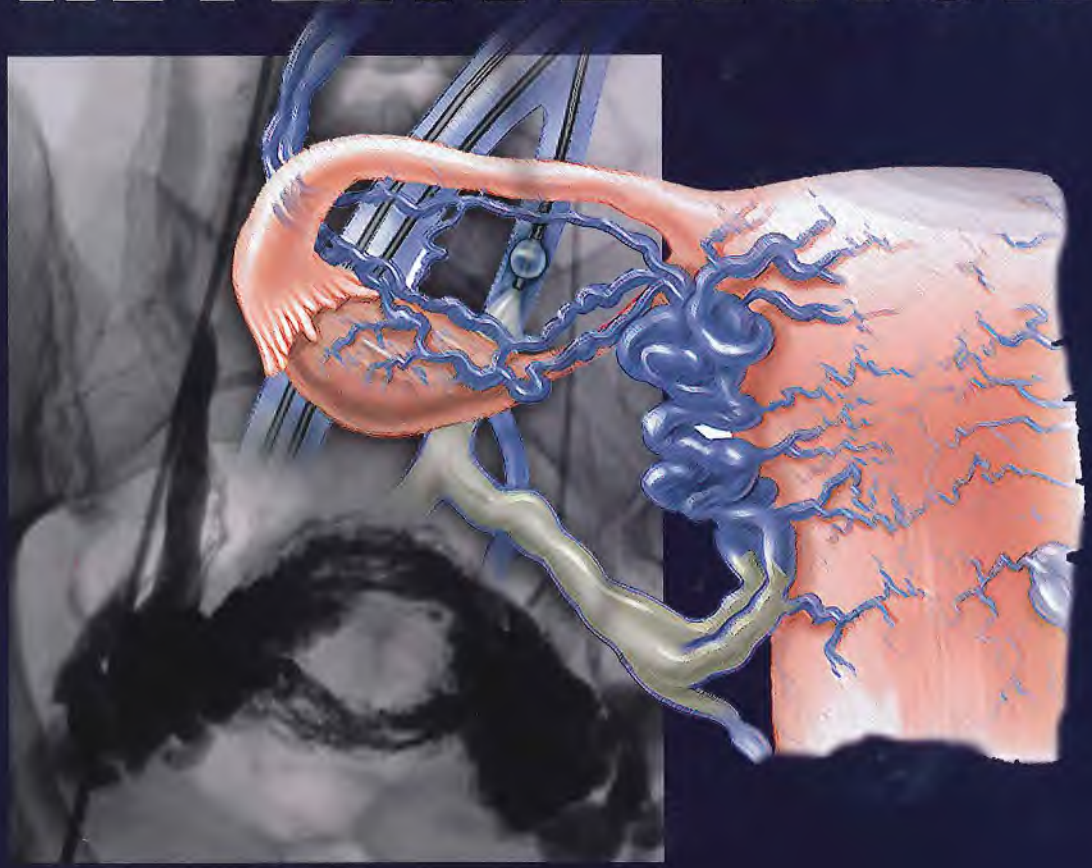
Exhibit A

MAURO | MURPHY | THOMSON
VENBRUX | MORGAN

IMAGE-GUIDED INTERVENTIONS

SECOND EDITION



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CHAPTER 86

Percutaneous Interventions for Acute Pulmonary Embolism

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Venous thromboembolism (VTE) is a global health problem that encompasses acute deep venous thrombosis (DVT) and acute pulmonary embolism (PE). Although the true incidence of PE is unknown, it is recognized as a significant cause of morbidity and mortality in hospitalized patients.[1] In the United States alone, it is estimated there are between 500,000 and 600,000 cases per year,[2] and approximately 300,000 people die every year from acute PE.[3] Indeed, acute PE is believed to be the third most common cause of death among hospitalized patients.[4]

Common risk factors for acute PE are related to underlying genetic conditions (e.g., factor V Leiden mutation, prothrombin 20210A mutation, and multiple other thrombophilias), acquired conditions (e.g., cancer, immobilization, trauma, surgery, prior DVT), and acquired hypercoagulable states (e.g., oral contraceptive use, nephrotic syndrome, antiphospholipid syndrome, disseminated intravascular coagulation, hyperestrogenic states, obesity).

There are three basic categories of acute PE: (1) *simple PE* with no associated heart strain and no hypotension, (2) *submassive PE* with associated right heart strain, (3) *massive PE* with associated right heart strain and hemodynamic shock. Patients with simple acute PE require treatment with therapeutic anticoagulation alone. Patients with submassive PE may require treatment escalation beyond anticoagulation; and patients with massive PE certainly require treatment escalation beyond anticoagulation alone.[5] The immediate mortality rate related to simple PE is less than 8% when the condition is recognized and treated with anticoagulation.[1,6,7] However, patients with submassive PE have a higher cumulative mortality rate, reaching approximately 20% over a 90-day period.[8] Patients with massive PE have the highest mortality rate, which can exceed 58%, including a high risk of sudden death.[9]

The pathophysiology of PE consists of direct physical obstruction of the pulmonary arteries, hypoxemic vasoconstriction, and release of potent pulmonary arterial vasoconstrictors that further increase pulmonary vascular resistance and right ventricular (RV) afterload. Acute RV pressure overload may result in RV hypokinesis and dilation, tricuspid regurgitation, and ultimately RV failure. RV pressure overload may also result in increased wall stress and ischemia by increasing myocardial oxygen demand while simultaneously limiting its supply. Ultimately, cardiac failure due to acute PE results from a combination of the increased wall stress and cardiac ischemia that compromise RV function and impair left ventricular (LV) output, resulting in life-threatening hemodynamic shock.[9] Depending on underlying cardiopulmonary reserve, patients with acute massive PE may deteriorate over the course of several hours to days and develop systemic arterial hypotension, cardiogenic shock, and cardiac arrest. Owing to the risk of sudden death, these critically ill patients with massive PE should be quickly identified as candidates for rapid endovascular treatment as a lifesaving procedure.[5]

INDICATIONS

Because of the high mortality associated with acute massive PE, successful management requires prompt risk stratification and decisive early intervention (Table 86-1). Confirmation of hemodynamic shock attributed to central obstructing embolus should be present to justify treatment escalation beyond anticoagulation. The American College of Chest Physicians has recommended that percutaneous catheter-directed therapy (CDT) be considered in acute massive PE patients who are unable to receive systemic thrombolytic therapy because of bleeding risk.[10] In addition, global meta-analytic data has demonstrated that percutaneous CDT can be considered as a first-line treatment option in lieu of intravenous (IV) tissue plasminogen activator (tPA) for patients with massive PE.[11]

Pulmonary angiography was once considered the gold standard for diagnosing PE, but it has largely been replaced by the wide availability of cross-sectional imaging. Historically, many types of imaging studies have been used in diagnosing acute pulmonary embolism, including ventilation/perfusion (V/Q) scanning, magnetic resonance angiography (MRA), and computed tomographic angiography (CTA). CTA is the preferred modality and has proven to be advantageous thanks to its wide availability, superior speed, characterization of nonvascular structures, and detection of venous thrombosis. CTA has the greatest sensitivity and specificity for detecting emboli in the main, lobar, or segmental pulmonary arteries. Systematic reviews and randomized trials suggest that outpatients with suspected pulmonary embolism and negative CTA studies have excellent outcomes without therapy.[12]

If a patient has either acute or chronic renal insufficiency and contrast administration is undesirable, echocardiography may be used to evaluate for right heart dysfunction as an indication for underlying acute PE. The echocardiogram can be performed at bedside, and the study may reveal findings that strongly support hemodynamically significant pulmonary embolism,[13] offering the potential to guide treatment escalation to thrombolytic and/or endovascular therapy. Large emboli moving from the heart to the lungs are occasionally confirmed with this technique. In addition, intravascular ultrasonography has also been used at the bedside to visualize central pulmonary emboli.[14]

Although the diagnosis of submassive PE follows a similar workup to evaluating massive PE, these patients do not present with systemic arterial hypotension, and particular attention must be paid to detecting the presence of right heart strain, which clinches the diagnosis of submassive PE. Identifying right heart strain allows risk stratification for

TABLE 86-1. Risk Stratification and Indications for Aggressive Intervention to Treat Massive Pulmonary Embolism

At least one of the following criteria must be present:
1. Arterial hypotension (<90 mmHg systolic or drop of > 40 mmHg)
2. Cardiogenic shock with peripheral hypoperfusion and hypoxia
3. Circulatory collapse with need for cardiopulmonary resuscitation

From Uflacker R. Interventional therapy for pulmonary embolism. J Vasc Interv Radiol 2001;12:147–64.

possible treatment escalation beyond anticoagulation in normotensive PE patients.[5] Echocardiography is the best imaging study to detect RV dysfunction in the setting of acute PE. Characteristic echocardiographic findings in patients with submassive PE include RV hypokinesis and dilatation, interventricular septal flattening and paradoxical motion toward the LV, abnormal transmitral Doppler flow profile, tricuspid regurgitation, pulmonary hypertension as identified by a peak tricuspid regurgitant jet velocity over 2.6 m/s, and loss of inspiratory collapse of the inferior vena cava (IVC).[15] An RV-to-LV end-diastolic diameter ratio of 0.9 or greater, assessed in the left parasternal long-axis or subcostal view, is an independent predictor of hospital mortality.[16] Detection of RV enlargement by chest CTA is especially convenient for diagnosis of submassive PE, because it uses data acquired during the initial diagnostic scan. Submassive PE can be diagnosed when RV enlargement on chest CT, defined by an RV-to-LV diameter ratio greater than 0.9, is observed[17]; RV enlargement on chest CTA also predicts increased 30-day mortality in patients with acute PE.[17,18] Even if shock and death do not ensue, survivors of acute submassive PE remain at risk for developing chronic PE and thromboembolic pulmonary hypertension.[19]

Additionally, monitoring cardiac troponin T (cTnT) identifies the high-risk group of normotensive patients with submassive PE.[20] A persistent increased cTnT level (>0.01 ng/mL) in PE patients with right heart strain predicts a significant risk of a complicated clinical course and fatal outcome, and these patients therefore require more aggressive treatment.[20] Identifying submassive PE for treatment escalation is important because these normotensive PE patients demonstrate increased short-term mortality and high risk of adverse outcomes when the degree of heart strain results in elevations in levels of cardiac troponins and brain-type natriuretic peptide.[21,22] The optimal protocol for treatment of acute submassive PE is still in evolution, but a proposed algorithm for managing submassive PE has been published[23] describing treatment escalation beyond anticoagulation (Fig. 86-1).

Based on the history, angiographic findings, and outcomes of patients undergoing CDT for acute PE, three groups of patients have been identified[24]:

- Type I patients with fresh clots that have recently embolized should respond well to mechanical thrombectomy with increased peripheral flow and oxygenation. In general, 2 to 3 weeks is the upper age limit of thrombus when considering the option of CDT.
- Type II patients with older and more organized clots respond less effectively to mechanical thrombectomy alone. Although more chronic clots are likely to remain, there is a chance for pulmonary flow improvement if pharmacologic thrombolysis of overlying acute thrombus can be achieved.
- Type III patients with organized chronic PE do not respond well to the effects of CDT.

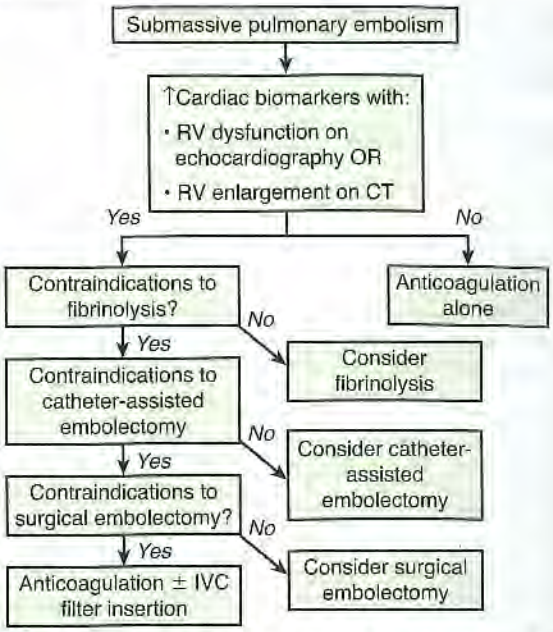

FIGURE 86-1. Algorithm for management of submassive pulmonary embolism patients. According to the algorithm, catheter-directed therapy should be considered in particular when there are contraindications to systemic thrombolysis. *CT,* Computed tomography; *IVC,* inferior vena cava; *RV,* right ventricle. *(From Piazza G, Goldhaber SZ. Management of submassive pulmonary embolism. Circulation 2010;122:1124–9.)*

CONTRAINDICATIONS

Because of the risk of major hemorrhage, aggressive anticoagulation, systemic thrombolysis, and local catheter-directed thrombolysis may be contraindicated in patients with recent major general or intracranial surgery. In such cases, mechanical methods of percutaneous catheter-directed thrombectomy, fragmentation, and/or aspiration should be considered without pharmacologic agents. Since pulmonary hypertension is a relative contraindication to pulmonary angiography, the degree of pulmonary hypertension and underlying cardiopulmonary reserve are important considerations prior to performing pulmonary angiography. These factors must be used to determine a safe rate and volume of contrast injection into the pulmonary circulation. For instance, when systolic pulmonary artery pressure (PAP) exceeds 55 mmHg, or right ventricular end diastolic pressure (RVEDP) is greater than 20 mmHg, the mortality associated with pulmonary angiography using large-volume power injection has been reported to be as high as 3%.[2,3] Therefore, such patients with massive PE should only receive a limited rate of power injection, controlled by hand. In the submassive PE patient, a selective contrast injection into the main left or right PA should not exceed a 20-mL volume at a rate of 10 mL/s. Lower injection parameters by hand may be considered depending on

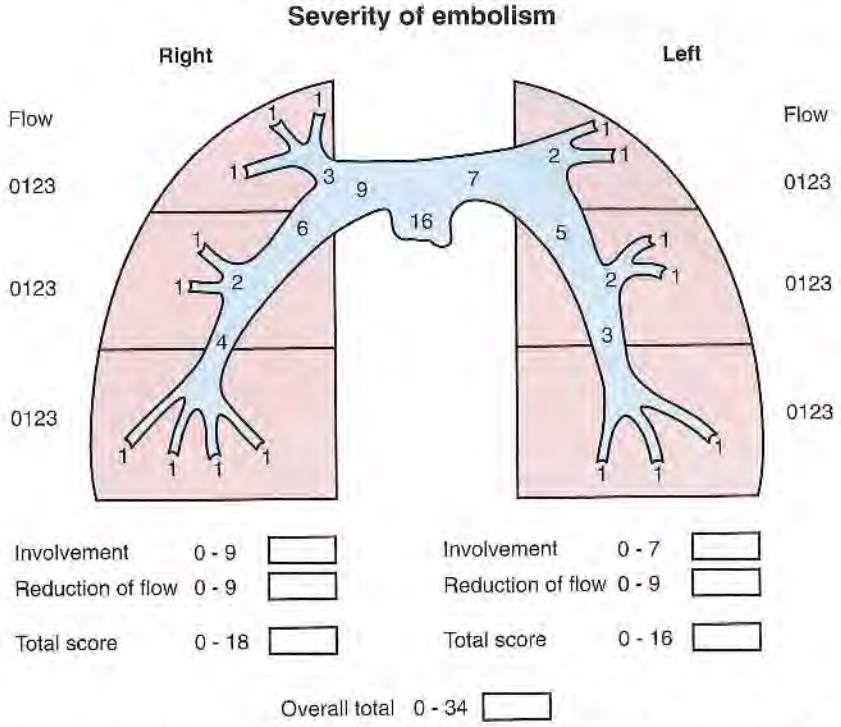

FIGURE 86-2. Schematic of pulmonary arterial segments used to grade severity of pulmonary embolism based on angiographic findings before and after treatment with thrombolytic and/or catheter-directed therapy. Segmental clot involvement and reduction of flow are scored separately. *(From Miller GAH, Sutton GC, Kerr IH, et al. Comparison of streptokinase and heparin in treatment of isolated acute massive pulmonary embolism. BMJ 1971;2:681–4.)*

degree of heart failure, as determined by the operator's judgment, to achieve adequate vessel opacification without endangering the patient. Pulmonary angiography can be used to calculate the degree of pulmonary obstruction before and after treatment, using the calculated Miller Index (Fig. 86-2). Finally, in PE patients with contraindications to anticoagulation and/or thrombolytic agents, placement of an IVC filter should be considered for prophylaxis of recurrent PE.

EQUIPMENT

Modern CDT for massive PE has been defined according to the following criteria: use of low-profile catheters and devices (≤10F), catheter-directed mechanical fragmentation and/or aspiration of emboli, and intraclot thrombolytic injection if a local drug is infused.[11] Therefore, a variety of devices can be successfully used to treat PE, so long as they meet criteria for modern CDT (Table 86-2).

Depending on anticipated bleeding risk, CDT may be performed with either no or low-dose local tPA injection. The initial goal of all these techniques is rapid debulking of central thrombus to relieve life-threatening heart strain, immediately improve pulmonary perfusion, and improve oxygenation (Fig. 86-3).[5]

In contrast to CDT for massive PE, which requires mechanical methods, the protocol for submassive PE consists of gentle image-guided infusion catheter placement and overnight pharmacologic thrombolysis without aggressive mechanical intervention. This treatment may be offered to patients who present primarily with submassive PE (Fig. 86-4), or as adjunctive treatment in patients with prior massive PE who have been "downstaged" via central clot debulking to submassive PE. For at least one of the access sites, it is preferable that the sheath be sized at least 2F larger than the infusion catheter to allow subsequent central pulmonary artery (PA) pressure measurements through the sheath. An 8F to 10F vascular sheath (e.g., Flexor sheath [Cook Medical, Bloomington, Ind.]) is recommended, and the sheath should be long enough to reach from the access point to the main pulmonary trunk. If a second sheath is placed for dual catheter infusions, the operator can decide on the specific diameter and length, based on vessel tortuosity, sufficient to provide stability for the second infusion catheter.

TECHNIQUE

Anatomy and Approaches

Solid catheter-based skills along with knowledge of the cardiopulmonary anatomy are important for safe intravascular placement and manipulation of catheters and thrombectomy devices. Catheterization of the PA can be performed using a variety of methods, depending on the operator's preference and experience. An example via the transfemoral approach is using a 5F or 6F pigtail catheter in conjunction with a hydrophilic Glidewire (Terumo Medical Corp., Somerset, N.J.) and torque control device. An example via the right transjugular approach is using a C2 catheter (Cook Medical) in conjunction with a Glidewire and torque control device. Regardless of technique used, the electrocardiogram should be continuously monitored by trained nursing staff. Catheterization should be meticulously performed to

TABLE 86-2. Catheter-Directed Therapy for Massive Pulmonary Embolism in 594 Patients

Author, Year (Reference)	Country	Patients, n	Sex-n	Age: Mean, Range	Technique-n	Local Intraclot Lytic During CDT-n	Local Intraclot Lytic, Extended Infusion-n	Minor Cxs	Major Cxs	Clinical Success (%)
Prospective Studies										
Schmitz-Rode et al. 1998[48]	Germany	10	M-6, F-4	54 (36-70)	PF-10	8	1	0	0	8/10 (80)
Schmitz-Rode et al. 2000[49]	Germany	20	M-10, F-10	59 (48-60)	PF-20	0	0	1	0	16/20 (80)
Muller-Hulsbeck et al. 2001[50]	Germany	9	M-4, F-5	55 (27-85)	ATD-9	0	5	0	0	9/9 (100)
Prokubovsky et al. 2003[51]	Russia	20	na	51 (32-75)	PF-20	0	16	0	0	14/20 (70)
Tajima et al. 2004[52]	Japan	25	M-8, F-17	61 (35-77)	PF & AT-25	25	21	0	0	25/25 (100)
Barbosa et al. 2008[53]	Brazil	10	M-7, F-3	57 (39-75)	PF-10, (ATD-na)	0	0	0	0	9/10 (90)
Retrospective Studies										
Brady et al. 1991[54]	England	3	M-0, F-3	36 (18-71)	PF-1, MC-2	2	2	0	0	3/3 (100)
Rafique et al. 1992[55]	South Africa	5	M-1, F-4	35 (21-47)	MC-5	5	5	1	0	5/5 (100)
Uflacker et al. 1996[24]	U.S.A.	5	M-4, F-1	45 (25-64)	ATD-5	1	1	0	1	3/5 (60)
Fava et al. 1997[32]	Chile	16	M-8, F-8	49 (20-68)	PF-16, (BA-na)	16	16	3	0	14/16 (88)
Stock et al. 1997[56]	Switzerland	5	M-3, F-2	50 (21-80)	PF & BA-5	5	5	0	2	5/5 (100)
Basche et al. 1997[57]	Germany	15	na	na (21-73)	PF & BA-2, BA-13	na	na	0	0	12/15 (80)
Hiramatsu et al. 1999[58]	Japan	8	M-4, F-4	58 (42-87)	AT & WD-8	0	8	0	0	7/8 (88)
Wong et al. 1999[59]	England	4	M-2, F-2	33 (18-46)	PF-1,PF & G-1, G-2	0	4	0	1	3/4 (75)
Murphy et al. 1999[60]	Ireland	4	M-2, F-2	60 (46-66)	MC & WD-4	4	4	0	0	4/4 (100)
Voigtlander 1999[61]	Germany	5	M-4, F-1	57 (25-72)	RT-5	0	0	4	0	3/5 (60)
Fava et al. 2000[62]	Chile	11	M-3, F-8	61 (37-79)	Hy-11	0	4	0	0	10/11 (91)
Egge et al. 2002[63]	Norway	3	M-2, F-1	49 (40-54)	PF-3	3	3	0	0	3/3 (100)
De Gregorio et al. 2002[33]	Spain	59	M-25, F-34	56 (22-85)	PF-52, PF & BA-4, PF & DB -3	59	57	8	0	56/59 (95)
Zeni et al. 2003[36]	U.S.A.	16	M-9, F-8	52 (30-86)	RT-16	0	10	2	1	14/16 (88)

TABLE 86-2. Catheter-Directed Therapy for Massive Pulmonary Embolism in 594 Patients—cont'd

Author, Year (Reference)	Country	Patients, n	Sex-n	Age: Mean, Range	Technique-n	Local Intraclot Lytic During CDT-n	Local Intraclot Lytic, Extended Infusion-n	Minor Cxs	Major Cxs	Clinical Success (%)
Reekers et al. 2003[64]	Netherlands	7	M-2, F-6	46 (28-76)	Hy-6, Oa-1	7	0	0	0	6/7 (86)
Tajima et al. 2004[65]	Japan	15	M-4, F-11	60 (27-79)	AT-15	9	0	0	0	15/15 (100)
Fava et al. 2005[66]	Chile	7	M-3, F-4	56 (30-79)	Hy-4, Oa-3	3	3	1	1	6/7/ (86)
Siablis et al. 2005[37]	Greece	6	M-4, F-2	59 (42-76)	RT-6	4	0	2	0	5/6 (83)
Yoshida et al. 2006[67]	Japan	8	M-4, F-4	61 (47-75)	PF & AT-8	na	na	0	1	7/8 (88)
Li J-J et al. 2006[68]	China	15	M-11, F-4	56 (19-73)	PF & ATD-13, PF & Hy-1, PF & Oa-1	6	0	0	0	15/15 (100)
Pieri and Agresti. 2007[69]	Italy	164	na	68 (35-78)	PF-164	164	164	0	0	138/164 (84)
Chauhan et al. 2007[70]	U.S.A.	6	M-2 F-4	64 (49-78)	RT-6	2	0	5	2	4/6 (67)
Krajina 2007[71]	Czech Rep	5	M-1, F-4	67 (52-80)	PF-3, PF & AT-2	3	0	0	0	2/5 (40)
Yang 2007[72]	China	19	M-13, F-6	62 (22-87)	PF-10, PF & AT-5, PF+SR-4	19	na	0	0	18/19 (95)
Margheri 2008[73]	Italy	20	M-12, F-8	66 (32-85)	RT-20	na	0	8	8	17/20 (85)
Vecchio et al 2008[38]	Italy	13	na	68 (54-80)	RT-13	na	0	6	8	8/13 (62)
Chen et al 2008[74]	China	26	M-15, F-11	53 (36-71)	ATD-17, SR-9	21	0	1	0	26/26 (100)
Eid-Lidt et al. 2008[35]	Mexico	18	M-6, F-12	51 (47-55)	PF-5, PF & SR-13	2	0	0	0	16/18 (90)
Kuo et al. 2008[31]	U.S.A.	12	M-7, F-5	56 (21-80)	PF & AT-6, PF & AT & BA-2, RT & AT-2, AT & IC-2	8	na	1	0	10/12 (83)
TOTAL = 35		594		53 (18-87)		356/535 67%	329/552 60%	(7.9%)* [5.0-11.3%]	(2.4%)* [1.9-4.3%]	(86.5%)* [82.2-90.2%]

*Pooled estimates from random effects model.
[%], 95% confidence intervals; *AT*, aspiration thrombectomy; *ATD*, Amplatz thrombectomy device (Microvena, White Bear Lake, Minn.); *B*, Dormia basket (Cook Europe, Bjaeverskov, Denmark); *BA*, balloon fragmentation; *Cxs*, complications; *G*, Gensini (Cordis Corp., Miami, Fla.); *Hy*, Hydrolyzer (Cordis Corp., Miami, Fla.); *IC*, infusion catheter; *MC*, multipurpose catheter; *na*, data not available; *Oa*, Oasis (Boston Scientific, Galway, Ireland); *PF*, pigtail fragmentation; *RT*, rheolytic AngioJet thrombectomy (Possis Medical, Minneapolis, Minn.); *SR*, Straub Rotarex (Straub Medical, Wangs, Switzerland); *WD*, wire disruption.
From Kuo WT, Gould MK, Louie JD, et al. Catheter-directed therapy for the treatment of massive pulmonary embolism: Systematic review and meta-analysis of modern techniques. J Vasc Interv Radiol 2009;20:1431–40.

minimize wire contact with cardiac structures to reduce the risk of ventricular tachycardia and vascular perforation while passing through the right heart and into the pulmonary trunk. Once the pulmonary outflow has been selected, depending on operator preference, the hydrophilic wire can be exchanged for a non-hydrophilic wire such as a 0.035-inch Rosen wire (Boston Scientific, Natick, Mass.) to provide stability for subsequent vascular sheath placement. Selective catheterization of the main right and left PAs is routinely performed, but selective and subselective

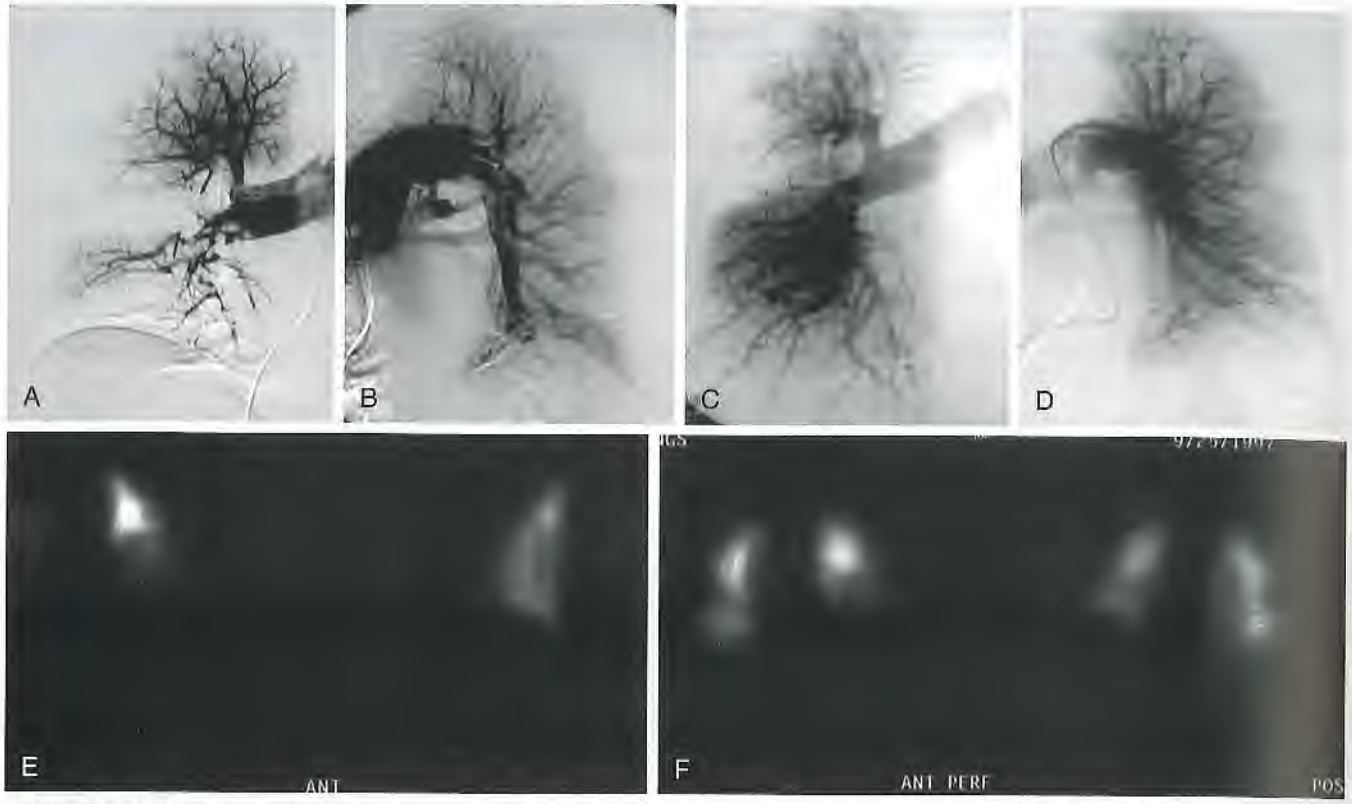

FIGURE 86-3. This patient with massive pulmonary embolism presented with syncope. **A,** Right pulmonary angiogram showed a large central embolism, with thrombus occluding most of the artery and sparing just a portion of the right upper lobe. **B,** Left pulmonary angiogram showed a large filling defect in main left pulmonary artery (PA). Catheter-directed therapy was initiated first to debulk central emboli. An infusion catheter was then wedged into main thrombus in the right PA, and urokinase was started at 100,000 IU/h for 36 hours, with alternating catheterization of the left PA for 12 hours. **C-D,** Posttreatment angiography showed significant improvement of bilateral pulmonary circulation. Patient experienced dramatic clinical improvement along with reduction of PA pressures. **E-F,** Pre- and post-treatment lung perfusion scans showed marked improvement in right lung perfusion, with some improvement in left lower lobe.

catheterization of pulmonary segments is often necessary for further treatment.

The femoral approach is preferred in most patients who are candidates for catheter-directed pulmonary thrombolysis or thrombectomy, but the right internal jugular approach is also feasible and may be preferred in the presence of IVC or iliofemoral thrombus. Most thrombectomy devices are easily passed from the right internal jugular vein into the right ventricle and PA.

Anticoagulation

Initial IV administration of heparin is the therapy of choice to treat all forms of acute pulmonary thromboembolism. Heparin binds to and accelerates the activity of antithrombin III, prevents additional thrombus formation, and permits endogenous fibrinolytic mechanisms to thrombolyse the clot that has already formed. During CDT for massive PE, full heparin anticoagulation may be continued during the clot debulking procedure. However, once the massive PE has been converted to submassive PE and overnight catheter-directed thrombolytic infusion is initiated, full heparin anticoagulation should be discontinued to minimize the risk of bleeding complications. During concomitant low-dose tPA infusion, a subtherapeutic heparin dose is desirable (partial thromboplastin time [PTT] < 60 seconds) to minimize risk of peri-sheath clot formation. To achieve this, the heparin infusion rate is typically between 300 and 500 units/h through a peripheral IV site. Once the patient has completed a course of catheter-directed thrombolytic therapy, full therapeutic anticoagulation can be resumed with full-dose IV heparin or low-molecular-weight heparin (LMWH). Full heparin anticoagulation should be maintained for 7 to 10 days as a bridge to subsequent oral anticoagulation.

Systemic Thrombolysis

Current approved medical therapy for acute massive PE consists of systemic thrombolysis with 100 mg of alteplase (Activase [Genentech, South San Francisco, Calif.]) infused IV over 2 hours,[3] and the most widely accepted indication for thrombolytic therapy in these patients is cardiogenic shock from acute PE. However, contraindications prevent many patients from receiving systemic thrombolysis. Even when patients with acute PE are prescreened for absolute contraindications, the rate of major hemorrhage from systemic thrombolytic administration is still about 20%, including a 3% to 5% risk of hemorrhagic stroke.[8,25] Furthermore, there may be insufficient time in the acute setting to infuse a full dose of IV thrombolytic.

In some instances, in appropriate candidates, it may be desirable to initiate IV tPA while simultaneously activating the interventional team to perform CDT. For example, in selected patients who are in extremis from PE and deemed candidates for any thrombolytic treatment, some clinicians

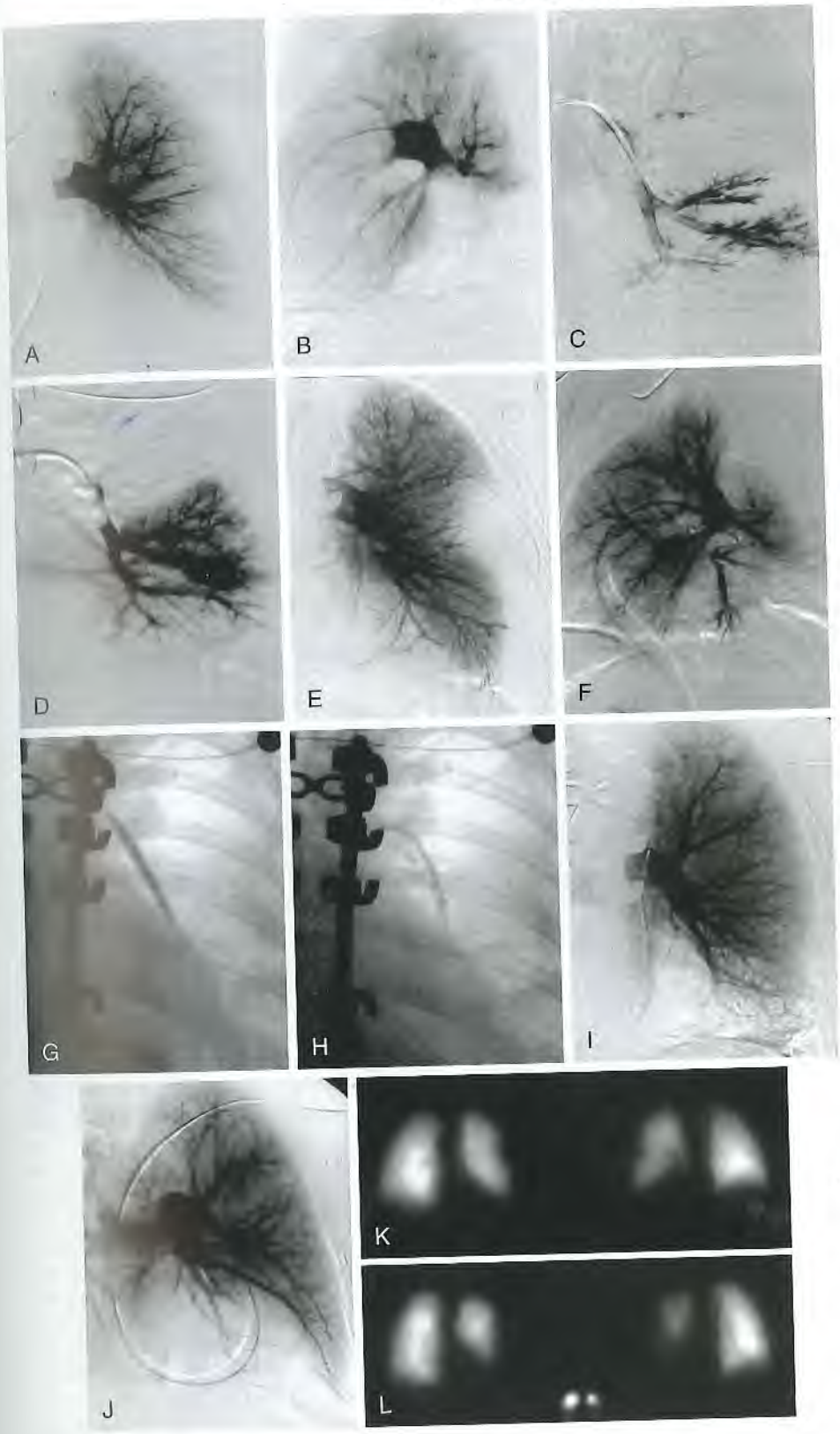

FIGURE 86-4. This 45-year-old woman with lymphoma presented with chest pain and dyspnea but remained hemodynamically stable; the diagnosis was acute submassive pulmonary embolism. **A,** Left pulmonary angiography showed occlusion of the posterior basal segment of the left lower lung. **B,** Lateral view of arteriogram showed occlusion of the posterior basal segment. Note patency of superior, anteromedial, and lateral basal segments, with a wedge of the posterior basal segment missing. **C,** An infusion catheter was carefully advanced into the posterior basal segment artery, and contrast medium injection showed extensive thrombosis. A catheter was wedged, and urokinase infusion was started. **D,** Follow-up angiography 12 hours into treatment showed restored patency of peripheral branches of the posterior basal segment, with persistent proximal occlusion of the posterior basal segment artery. **E-F,** Anterior and lateral views of a 24-hour follow-up angiogram showed persistent proximal occlusion and increased volume of a pleural effusion, with further collapse of the superior segment and left upper lung. **G-H,** Balloon angioplasty and occlusion balloon thrombectomy was performed in the persistently occluded segment of the posterior basal segment resulting in recanalization. **I-J,** Follow-up left pulmonary angiogram 1 month after treatment showed a patent posterior basal segment. **K,** Pretreatment lung perfusion scan showed reduced perfusion of the left lower lobe. **L,** Posttreatment scan showed persistent reduced perfusion of the left lung base due to an underlying pleural effusion.

may wish to initiate urgent "medical" treatment in the form of IV thrombolytic as a bridge to escalation "surgical" treatment with CDT. When used in this fashion, IV tPA could also be less risky. For instance, the amount of IV thrombolytic could be reduced by at least 50% (from the standard 100 mg tPA dose infused over 2 hours) if catheter intervention is initiated promptly, allowing discontinuation of IV tPA within 30 to 60 minutes.[26]

Catheter-Directed Thrombolysis

Under the definition of modern CDT,[11] two basic protocols of catheter-directed thrombolysis have emerged for

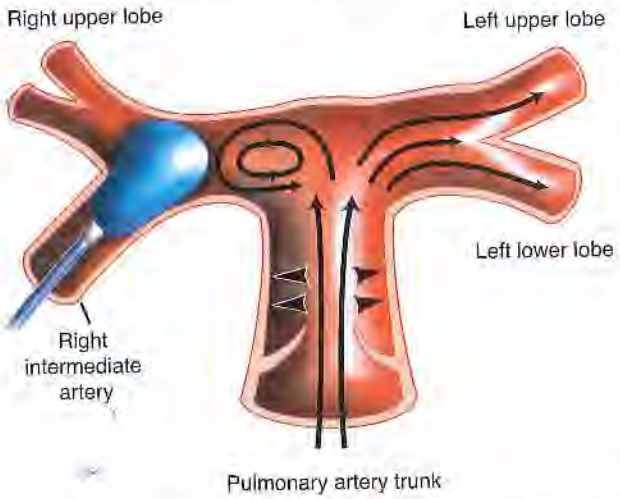

FIGURE 86-5. Schematic drawing of a pulmonary arterial flow model showing vortex formation immediately proximal to the level of obstruction. Note prominent vortex near the occlusion causing most circulating fluid to flow toward the nonoccluded left pulmonary artery. There is minimal fluid contact with the occluding embolus (the balloon). *(From Schmitz-Rode T, Kilbinger M, Günther RW. Simulated flow pattern in massive pulmonary embolism: Significance for selective intrapulmonary thrombolysis. Cardiovasc Intervent Radiol 1998;21:199–204.)*

treatment of massive and submassive PE, respectively. For massive PE, a catheter-directed bolus of thrombolytic drug is used in conjunction with mechanical clot fragmentation and/or aspiration to achieve central clot debulking. Depending on anticipated bleeding risk, CDT may be performed with either no or low-dose local tPA injection. The goal of these techniques is rapid central clot removal to relieve life-threatening heart strain and immediately improve pulmonary perfusion. Catheter intervention is important not only for creating an immediate flow channel through the obstruction, but also for exposing a greater surface area of thrombus to the effects of locally infused thrombolytic drug. If thrombolysis is performed without intraclot drug injection, and if the thrombolytic is instead infused proximal to the target embolus (as performed in older studies), there is little added benefit compared to systemic IV infusion.[27] Schmitz-Rode et al. demonstrated with in vitro and in vivo flow studies[28] that an obstructing embolus causes proximal vortex formation that prevents a drug infused upstream from making rapid contact with the downstream embolus, and the eddy currents instead cause washout of thrombolytic into the unobstructed pulmonary arteries (Fig. 86-5). These flow studies emphasize the importance of direct intrathrombus injection as an adjunct to embolus fragmentation to achieve rapid and effective catheter-directed thrombolysis.[28]

Several devices meeting criteria for modern CDT have been used effectively, but the most common technique is rotating pigtail fragmentation, which has been used either alone or in combination with other methods in 70% of patients worldwide receiving CDT.[11] Although pigtail clot fragmentation appears to effectively debulk proximal emboli, in some instances it has resulted in distal embolization with PAP elevation, requiring adjunctive aspiration thrombectomy to complete treatment.[29] Aspiration can be performed with virtually any end-hole catheter, such as an 8F JR4 catheter (Cook Medical). Additional clot fragmentation may also be achieved with insertion and inflation of an angioplasty balloon sized below the target arterial diameter (Fig. 86-6). Thus it is important to have adjunctive methods available to use in conjunction with pigtail rotation. The main advantage of the rotating pigtail is its wide availability and low cost relative to the mechanically-driven thrombectomy devices.

For treatment of submassive PE, or once massive PE has been downstaged to submassive PE, further mechanical debulking is usually unnecessary, and the protocol consists of careful image-guided infusion catheter placement into thrombosed segments for overnight pharmacologic thrombolysis.[5] Once the infusion catheters have been properly positioned and connected to IV pumps, catheter-directed thrombolysis should be initiated using alteplase at a rate of 0.5 mg/h through the drug lumen of each catheter if bilateral catheters are used. If only one catheter has been placed for unilateral treatment, the rate may be increased to 1 mg/h through the single infusion catheter. The recommended total tPA infusion rate should be 1 mg/h. To achieve the infusion dose, the reconstituted drug can be diluted in normal saline solution to yield a concentration of 0.1 mg tPA/mL of solution, and the pump can be set accordingly to deliver the prescribed dose. An alternative to catheter-directed tPA is urokinase infusion. The regimen consists of a bolus infusion of 200,000 to 500,000 IU followed by an infusion of 100,000 IU/h of urokinase for 12 to 36 hours.[30] Fibrinogen levels can be monitored, particularly in those patients at greater risk of bleeding or if the infusion will be continued beyond 24 hours. When fibrinogen levels drop below 150 to 200 mg/dL, the infusion should be reduced, discontinued, or alternatively continued with transfusions of fresh frozen plasma if further thrombolysis is desired.[5]

Catheter-Directed Embolectomy, Fragmentation, and Thrombolysis

Contrary to invasive open surgical thrombectomy, which has been associated with high perioperative morbidity and mortality, percutaneous CDT represents a safe, less invasive option for treating patients with acute massive PE.[11] As mentioned, the rationale for using percutaneous devices in the pulmonary circulation is rapid central clot debulking to relieve life-threatening heart strain and immediately improve pulmonary perfusion, which can be immediately verified by follow-up angiography and hemodynamic assessments. Percutaneous embolectomy, clot fragmentation, and mechanical thrombolysis also serve to expose a greater surface area of thrombus to the effects of locally infused thrombolytic drug. However, depending on anticipated bleeding risk, CDT may be performed with either no or low-dose local tPA injection, depending on operator preference and risk assessment. Regardless of the decision to use thrombolytic drug, CDT can be used effectively when full-dose thrombolytic therapy is contraindicated or fails to resolve hemodynamic shock.[3,5,11]

An ideal percutaneous thrombectomy device for treating PE should have these characteristics:

- Low profile (≤10F) and long enough to reach the PA from a peripheral venous access site

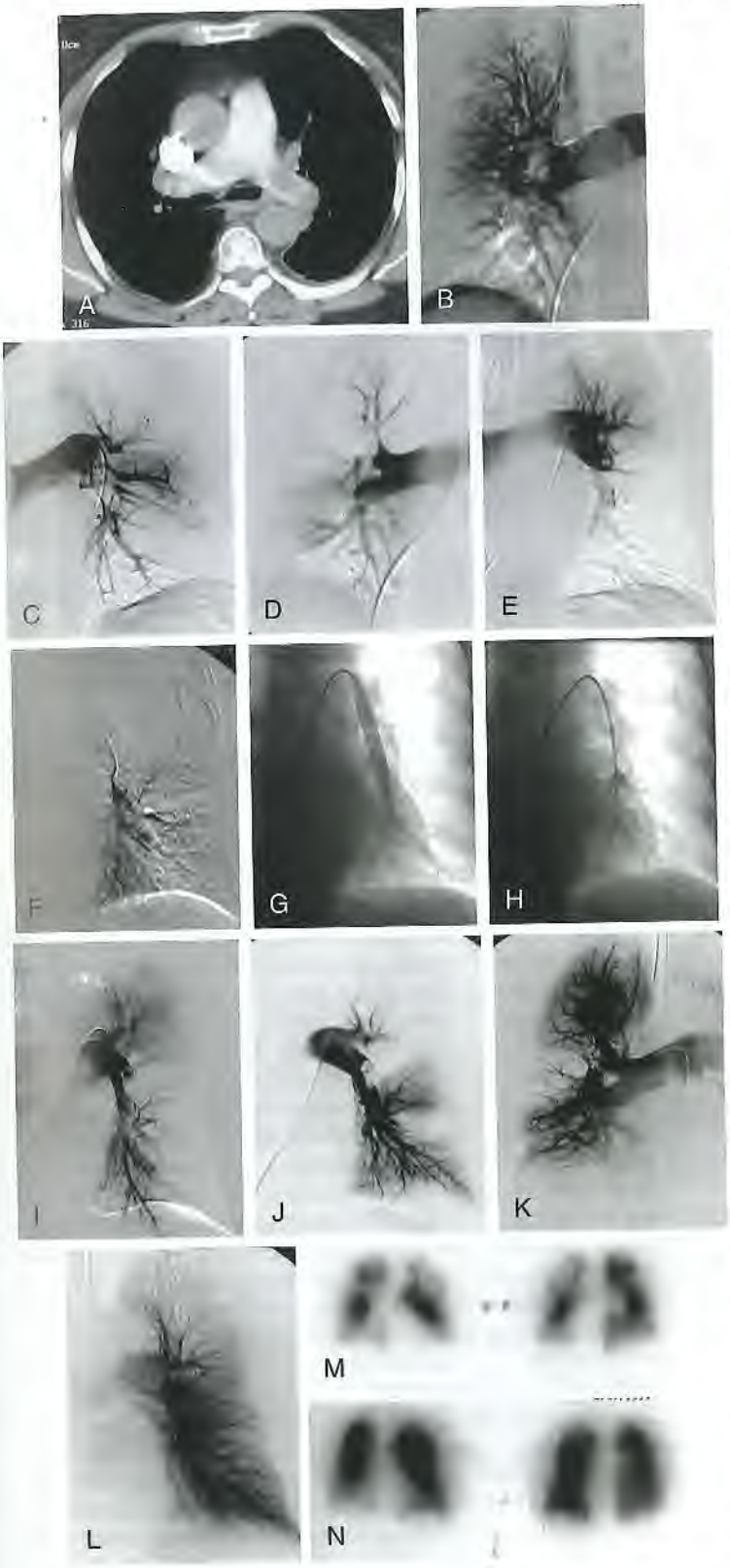

FIGURE 86-6. This 78-year-old woman with chronic obstructive pulmonary disease and history of myocardial infarction 1 month earlier presented to the emergency department with symptoms of deep vein thrombosis, chest pain, shortness of breath, and congestive heart failure. Chest computed tomographic angiography (CTA) was positive for acute pulmonary embolism. Ventilation/perfusion scan showed massive perfusion defects. Patient was transferred to our hospital, and a pulmonary arteriogram was requested for possible catheter-directed treatment. **A,** Chest CT scan showed large filling defects in both main pulmonary arteries. After hemodynamic stabilization, a pulmonary arteriogram was performed. **B,** Right pulmonary angiogram showed severe obstruction at the bifurcation of the right main pulmonary artery (PA). There was reduced perfusion of the right upper lobe and marked hypoperfusion of the right lower lobe. **C,** Left pulmonary angiogram showed a large embolism involving the left lower lobe with marked reduction in peripheral perfusion. Pulmonary artery pressure (PAP) was 39 mmHg. **D,** Follow-up right pulmonary angiogram after 15 hours of catheter-directed thrombolytic infusion showed marked improvement of the obstruction, with some residual clots involving the right upper and middle lobes. There was interval improvement in right lower lobe perfusion. **E,** Follow-up left pulmonary angiogram showed progressive occlusion of the left lower lobe likely from distal migration of a proximal thrombus. PAP was 46 mmHg. **F,** Selective catheterization of the left lower lobe branch through the clot was performed and showed total occlusion of the lower lobe artery. **G,** A 10-mm balloon catheter was advanced into the lower lobe branches over a wire and used to fragment clot. **H,** An occlusion balloon was trawled back several times to further fragment the clots. **I,** An angiogram after mechanical balloon thrombectomy showed improved lower lobe segment patency. A catheter was placed within the partially occluded artery, and thrombolytic infusion was continued. **J,** Follow-up left pulmonary angiogram after 15 hours of local thrombolytic infusion showed significant improvement in left lung perfusion. **K,** Final right pulmonary angiogram showed significant improvement in right pulmonary perfusion. **L,** Final left pulmonary angiogram showed near complete patency of the left PA and peripheral branches. Mean PAP after treatment was 33 mmHg. The patient improved clinically, was weaned off the ventilator, and successfully extubated. **M,** Pretreatment perfusion scan showed multiple wedge-shaped areas of segmental hypoperfusion. **N,** Perfusion scan 3 days after catheter-directed thrombolytic therapy showed remarkable improvement in bilateral pulmonary perfusion. After discharge from the intensive care unit, the only complication was acute renal failure that eventually resolved after 5 days, with return of creatinine to normal levels. The patient was discharged home within 1 week after receiving catheter-directed therapy.

- Adequate flexibility for facile insertion and navigation in the pulmonary circulation
- Capable of achieving embolectomy, clot fragmentation, and/or mechanical thrombolysis in a large vessel
- Allows concomitant intraclot thrombolytic drug injection if desired
- Safe in the central circulation, with low risk of vascular perforation, no widespread distal embolization, and no hemolytic side effects

Since no current device possesses all these characteristics, a combination of devices and methods can be used to achieve effective CDT.

FIGURE 86-7. Photo diagram of the rotating pigtail method most commonly used to treat acute massive pulmonary embolism. *(From Schmitz-Rode T, Janssens U, Duda SH, et al. Massive pulmonary embolism: Percutaneous emergency treatment by pigtail rotation catheter. J Am Coll Cardiol 2000;36:375–80.)*

FIGURE 86-8. Close-up photo of the Aspirex device tip. *(Courtesy Straub Medical AG, Wangs, Switzerland.)*

Percutaneous Devices and Methods

Rotating Pigtail Clot Fragmentation

The most common technique currently used is rotating pigtail fragmentation (Fig. 86-7), which has been used either alone or in combination with other methods in 70% of patients worldwide receiving CDT.[11] Although a robust pigtail has been manufactured in Europe specifically for treating PE (Cook Europe, Bjaeverskov, Denmark), virtually any type of pigtail catheter can be used. The pigtail catheter and its distal side holes can also be used to inject local thrombolytic drug directly into the thrombus. Although pigtail clot fragmentation appears to effectively debulk central emboli, in some instances it has resulted in distal embolization with PAP elevation, requiring adjunctive aspiration thrombectomy to complete treatment.[29]

Balloon Angioplasty for Clot Fragmentation

Additional clot fragmentation may also be achieved with insertion and inflation of an angioplasty balloon sized below the target arterial diameter. Specifically, mechanical clot fragmentation has been described using angioplasty balloons between 6 and 16 mm in diameter. When used in conjunction with local pharmacologic thrombolysis for massive PE, these methods have been very successful, with an 87.5% recovery rate, as measured by PAPs, blood O_2 values, and clinical outcomes.[32,33]

Simple Aspiration Thrombectomy

Aspiration can be performed with virtually any end-hole catheter, such as an 8F JR4 catheter (Cook Medical) or 10F Pronto catheter (Vascular Solutions, Minneapolis, Minn.). This method works best on central occlusive thrombus and should be used in conjunction with the methods already mentioned.

Electronic Aspiration Thrombectomy

The Aspirex (Straub Medical, Wangs, Switzerland), has shown promising results for acute PE thrombectomy.[34,35] This device works on the principle of a rotating Archimedes screw that resides within a low-profile catheter lumen (Fig. 86-8). The metallic spiral is connected to an electric motor drive and control unit. Electronic activation of the spiral coil produces aspiration from the open catheter tip, transporting material down the catheter shaft and into a collecting system.

High-Rpm Mechanical Thrombectomy

The Helix Clot Buster (ev3/Covidien, Plymouth, Minn.), formerly known as the *Amplatz thrombectomy device* (ATD), has been used to treat acute PE. The device is a 75- or 120-cm-long, 7F reinforced polyurethane catheter with a distal metal tip containing an impeller connected to a drive shaft. The catheter is connected to an air source turbine that generates up to 140,000 rpm at pressures between 30 and 35 psi during operation. Although little data are available on the new version of this device for treatment of PE, data from off-label use of the older 8F version have been published, with use in conjunction with a 10F guide catheter.[24] The possibility of hemolytic complications exists, but so far the degree has not been shown to be clinically significant.[24] Despite promising results, production of the Helix device is currently on hold by the manufacturer, with possible plans for a product re-release.

Rheolytic Thrombectomy

The mechanism of rheolytic thrombectomy is a high-pressure saline jet in conjunction with aspiration. This creates a Venturi effect that causes fragmentation and aspiration of the clot. The AngioJet (Possis Medical, Minneapolis, Minn.) is a double-lumen system with diameters ranging from 4F to 6F. Although results were promising in early small series of patients with massive PE,[36-38] recent meta-analytic data revealed higher procedure-related complications associated with AngioJet rheolytic thrombectomy (ART), including bradyarrhythmia, heart block, hemoglobinuria, renal insufficiency, major hemoptysis, and procedure-related death. Several deaths related to the AngioJet have been recorded in the U.S. Food and Drug Administration's (FDA's) MAUDE (Manufacturer and User

Facility Device Experience) database.[39] As a result, the FDA has issued a black-box warning on the device label.[40] For all these reasons, the AngioJet device should probably be avoided as the initial mechanical option in CDT protocols for acute massive PE.[26,41]

Pulmonary Artery Stent Placement

Case reports have described the use of metallic stents in critically ill patients with persistent central obstruction from presumed chronic emboli resistant to catheter-directed thrombolysis. The stents have been placed alongside organized PA emboli in which the patients presented with cor pulmonale, profound arterial hypoxemia, and hypotension that did not respond to other therapies.[42,43] The paucity of evidence should make use of stents only considered when there is life-threatening PE refractory to CDT (described earlier).

Ultrasound-Assisted Catheter-Directed Thrombolysis

The EKOS infusion catheter (EKOS Corp., Bothell, Wash.) uses microsonic energy designed to help loosen and separate fibrin to enhance clot permeability while increasing availability of more plasminogen activation receptor sites for tPA. The microsonic energy is also intended to drive the thrombolytic agent deep into the blood clot to accelerate thrombolysis.[44] If successful, it has the potential to shorten the duration of infusion and lower the total dose of thrombolytic drug in submassive PE patients.[44]

CONTROVERSIES

In 1988, Verstraete et al. published a study[27] comparing the recanalization effects of intrapulmonary versus IV infusion of rtPA and showed that transcatheter intrapulmonary delivery did not offer a significant benefit over the IV route. The major flaw in the study was that intrapulmonary drug delivery was performed proximal to the target clot, without intraclot thrombolytic injection and without mechanical intervention. As noted earlier, subsequent in vitro and in vivo flow studies[28] confirmed that an obstructing embolus causes proximal vortex formation that prevents a drug infused upstream (even via catheter) from making rapid contact with the downstream embolus, and the eddy currents instead cause washout of thrombolytic into the unobstructed pulmonary arteries (see Fig. 86-5). This emphasizes the importance of *direct* intrathrombus injection as an adjunct to embolus fragmentation to achieve rapid and effective catheter-directed thrombolysis.[28]

Despite the complications associated with AngioJet rheolytic thrombectomy and the FDA black box warning, some interventionalists continue to use this device to treat acute PE.[26] A meta-analysis of data on CDT[11] revealed that the highest complication rates occurred in patients treated with ART, including a 40% rate of minor complications and 28% rate of major complications that included procedure-related death.[11] Cumulative data indicate that most modern CDT (89%) has been performed worldwide with a high degree of safety and efficacy *without* using ART.

OUTCOMES

In a systematic review and meta-analysis of 594 patients with acute massive PE treated with modern CDT, clinical success was achieved in 86.5% (Fig. 86-9), where success was defined as stabilization of hemodynamics, resolution of hypoxia, and survival to hospital discharge.[11] In the same study, 96% of patients received CDT as the first adjunct to heparin, with no prior systemic tPA infusion, and 33% of cases were initiated with mechanical treatment alone without local thrombolytic infusion.[11] The data were derived across 18 countries from 35 studies—six prospective, 29 retrospective—and pooled results were similar in prospective versus retrospective studies, with no statistically significant difference. The pooled frequency of success was higher in studies in which at least 80% of participants received local thrombolytic therapy during the procedure (91.2% vs. 82.8%). The pooled frequency of success was also higher in studies in which at least 80% of participants received extended local thrombolytic therapy for treatment of residual submassive PE (89.2% vs. 84.2%).[11]

Modern CDT continues to be used worldwide. In 2011, another large-scale study of 111 PE patients confirmed that modern catheter-directed thrombolysis with mechanical fragmentation achieves rapid normalization of the pulmonary pressure and is a safe and effective method for treating acute massive PE.[30] Patients in extremis from massive PE require emergent treatment escalation beyond anticoagulation, and if IV tPA is contraindicated or there is insufficient time for full-dose tPA, CDT may be the only viable treatment option. Indeed, at experienced centers, the use of modern CDT has proven to be a lifesaving treatment in patients dying from acute massive PE.[11,30]

Submassive Pulmonary Embolism

There is growing evidence that aggressive treatment of submassive PE is beneficial. The Management Strategies and Prognosis of Pulmonary Embolism Trial-3 (MAPPET-3) randomized 256 patients with submassive PE to receive 100 mg of IV tPA over a 2-hour period, followed by unfractionated heparin infusion, versus placebo plus heparin anticoagulation.[45] Compared with heparin anticoagulation alone, thrombolysis resulted in a significant reduction in the primary study endpoint of in-hospital death or clinical deterioration that required escalation of therapy (defined as catecholamine infusion, rescue thrombolysis, mechanical ventilation, cardiopulmonary resuscitation, or emergency surgical embolectomy).[45] The difference was largely attributable to a higher frequency of open-label thrombolysis (breaking randomized trial protocol to offer medically necessary thrombolysis) due to clinical deterioration as determined by the treating clinician.[45]

In a prospective study of 200 patients with submassive PE,[19] echocardiography was performed at the time of diagnosis and after 6 months to determine the frequency of pulmonary hypertension between two groups—one group treated with heparin and another group treated with IV tPA and heparin. The median decrease in PA systolic pressure was only 2 mmHg in patients treated with heparin alone, compared with 22 mmHg in those treated with tPA plus heparin.[19] At 6 months, the PA systolic pressure increased in 27% of patients who had received heparin alone, and nearly half of those patients were moderately symptomatic.[19] These data suggest that thrombolytic therapy may reduce the likelihood of developing chronic thromboembolic pulmonary hypertension.[19]

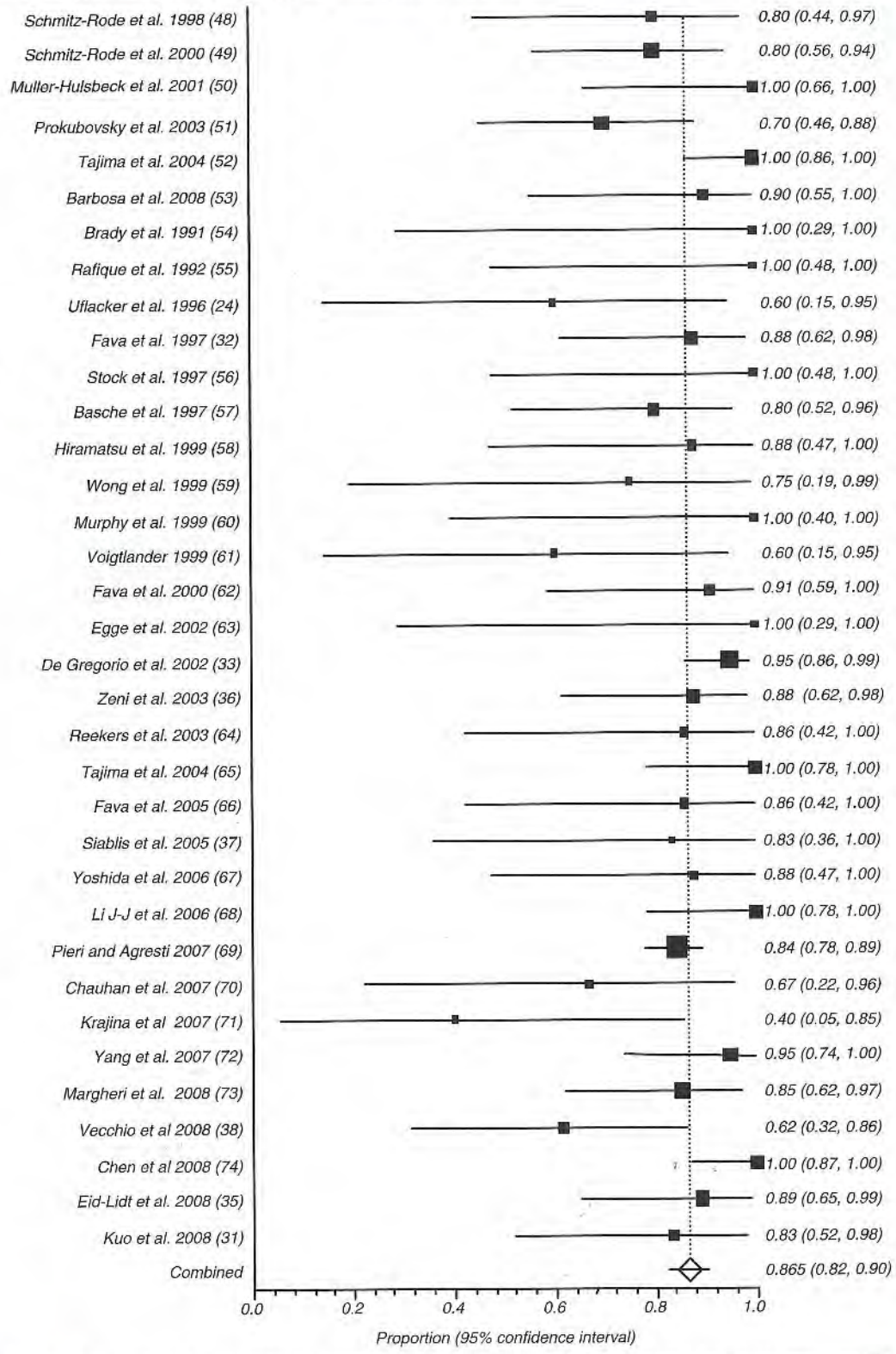

FIGURE 86-9. Forest plot shows clinical success rates from CDT and confidence intervals (CIs) from reported studies encompassing 594 patients with acute massive pulmonary embolism. Percentage clinical success is denoted along x-axis. Extended lines represent 95% CIs. Squares are proportional to study weight. Width of diamond corresponds to 95% CI for pooled clinical success rate of 86.5%. *(From Kuo WT, Gould MK, Louie JD, et al. Catheter-directed therapy for the treatment of massive pulmonary embolism: Systematic review and meta-analysis of modern techniques. J Vasc Interv Radiol 2009;20:1431–40.)*

However, for patients who are not good candidates for systemic tPA, the next logical step to consider is catheter-directed intervention. That is why the incorporation of a CDT protocol with targeted drug delivery and a lower overall thrombolytic dose could further improve outcomes while reducing hemorrhagic risk in the submassive PE group.[5] Indeed, when low-dose (≤30 mg) local tPA was administered to acute massive PE patients—a group at higher risk for bleeding than submassive PE patients[12]—there were no major hemorrhagic complications.[10,11] Furthermore, when patients with massive PE are downstaged to submassive PE via initial catheter-directed treatment of central clot, the overall clinical success was higher when these patients also received extended local thrombolytic therapy.[11] Such results strongly suggest that use of endovascular treatment in the form of local thrombolytic infusion appears to be a promising option for reducing both acute and chronic complications from PE, while avoiding the bleeding risks associated with full-dose systemic thrombolysis.

COMPLICATIONS

From the global meta-analysis on CDT,[11] the pooled risk of major complications was only 2.4%. Among 594 patients, major procedural complications occurred in 25 patients, including 11 groin hematomas (requiring transfusion), five noncerebral hemorrhages (sites unspecified, requiring transfusion), two cases of massive hemoptysis requiring transfusion, one renal failure requiring hemodialysis, one cardiac tamponade treated with surgical repair, one death from bradyarrhythmia and apnea, one death from widespread distal embolization, one death associated with cerebrovascular hemorrhage, and two procedure-related deaths (mechanism unspecified). The highest complication rates occurred in the 68 patients who underwent CDT with the rheolytic AngioJet device, including 27 minor complications (40%) and 19 major complications (28%).[11] The complications of bradyarrhythmia, heart block, hemoglobinuria, temporary renal insufficiency, one minor hemoptysis, one major hemoptysis, five major hemorrhages, and five procedure-related deaths were all associated with the AngioJet device. Interestingly, 76% of the recorded major complications (19/25) in the study were directly attributed to ART, despite the fact that it was used in only a small percentage (11%) of the 594 patients evaluated.[11] Conversely, the data indicated that most modern CDT (89%) was performed worldwide with a high degree of safety and efficacy without using ART.

Overall, compared to the high rate of major hemorrhagic complications from systemic tPA of 20%,[8,25] the rate of major complications from modern CDT has proven to be only 2.4%.[11] Since most of these complications were attributed to ART, elimination of AngioJet from the CDT protocol could further improve the overall safety of modern CDT.

POSTPROCEDURAL ANTICOAGULATION AND FOLLOW-UP CARE

Therapeutic anticoagulation is the primary medical treatment for all patients diagnosed with acute VTE, and it should be prescribed for at least 3 to 6 months or indefinitely, depending on careful assessment of several factors.[10] If VTE is associated with a major irreversible risk factor such as cancer, these patients have at least a 15% risk of recurrence during the first year after stopping anticoagulation.[46] Consequently, patients with active cancer and a first episode of VTE usually receive treatment indefinitely.[10] Conversely, if VTE is provoked by a major reversible risk factor such as recent surgery, the risk of recurrence is about 3% in the first year if anticoagulation is discontinued after 3 months.[46] Between these two extremes are patients who have suffered acute VTE associated with a minor reversible risk factor (e.g., estrogen therapy or soft-tissue leg injury) and those who have had an unprovoked or idiopathic VTE.[47] For patients with a minor reversible risk factor, the risk of recurrence is about 5% in the first year after stopping anticoagulant therapy.[47] This is considered low enough to justify stopping anticoagulant therapy at the end of 3 months.[10] However, an unprovoked proximal DVT or PE has a higher risk of recurrence (about 10% in the first year after stopping therapy).[46] Continuing anticoagulant therapy beyond 3 months confers a greater than 90% risk reduction for preventing recurrence among these patients; however, if anticoagulants are subsequently stopped after 6 or 12 months of treatment, the risk of recurrence appears to be the same as if anticoagulants had been stopped after 3 months.[10] This high risk of recurrence is indirect evidence that patients with a first unprovoked proximal DVT or acute PE should receive anticoagulant therapy indefinitely. However, after all the major risks and benefits of long-term anticoagulation therapy have been explained, patient preference should also influence the decision.[46] Because of all these complexities, consultation with a hematologist or physician experienced in treating VTE is essential in determining the optimal anticoagulation regimen.

If there are contraindications to immediate anticoagulation for acute VTE, IVC filtration may be indicated. For those patients who have suffered near death from massive PE, IVC filter placement should be considered in addition to anticoagulation. For those diagnosed with submassive PE, it is unclear whether additional filter placement is necessary in addition to anticoagulation. If caval filtration is desired, a retrievable filter is often preferable, since it has the option to be removed. When lifelong filtration is not intended, such patients should be followed closely and scheduled for timely filter removal (e.g., once they are stabilized on therapeutic anticoagulation). Once filtration is no longer indicated, successful IVC filter removal can spare patients the potential risks associated with long-term filter implantation.

KEY POINTS

- Rapid risk stratification by identifying acute massive and acute submassive pulmonary embolism (PE) patients is essential in determining appropriate treatment escalation beyond anticoagulation.
- For patients with less severe or submassive PE (defined by right heart strain), endovascular treatment in the form of local thrombolytic infusion appears to be a promising option for reducing both acute and chronic complications from PE while avoiding the bleeding risks associated with full-dose systemic thrombolysis.
- For patients in extremis from massive PE (defined by hemodynamic shock), emergent treatment escalation is necessary

in the form of catheter-directed therapy (CDT) for rapid debulking of central obstructive emboli, especially if systemic tissue plasminogen activator (tPA) is contraindicated.

- CDT may be the only viable option for rapid restoration of pulmonary arterial flow if intravenous systemic tPA is contraindicated or has already failed to resolve hemodynamic shock.
- Rheolytic thrombectomy with the AngioJet device has been associated with a high rate of major complications, including procedure-related death, so to improve the overall safety of modern CDT, it should probably be avoided in future protocols.
- The major complication rate from CDT is only 2.4%, versus the 20% rate of major hemorrhage associated with systemic tPA infusion.
- At experienced centers, the use of modern CDT has proven to be a lifesaving treatment for acute massive PE, with an overall clinical success rate of 86.5%.
- Following intervention, therapeutic anticoagulation should be continued as the ongoing medical treatment, and duration of therapy must depend on careful assessment of several risk factors.

▸ SUGGESTED READINGS

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